TRANSCRIPT OF PROCEEDINGS

IN THE MATTER OF:)
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STAKEHOLDERS MEETING WITH)
OREGON STATE UNIVERSITY)
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Pages: 1 through 56

Place: Riverdale, MD

Date: February 27, 2004

HERITAGE REPORTING CORPORATION
Official Reporters
1220 L Street, N.W., Suite 600
Washington, D.C. 20005-4018
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UNITED STATES DEPARTMENT OF AGRICULTURE

IN THE MATTER OF:)
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STAKEHOLDERS MEETING WITH)
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Training Room 1
4700 River Road
Riverdale, MD

Friday,
February 27, 2004

The parties met, pursuant to the notice, at 4:08 p.m.

BEFORE: MS. CINDY SMITH
Deputy Administrator

APPEARANCES:

For the U.S. DEPARTMENT OF AGRICULTURE:

REBECCA BECH, Assistant Deputy Administrator
JOHN TURNER
NEIL HOFFMAN
MICHAEL WACH
SUSAN KOEHLER

Meeting with: Oregon State University
Steven H. Strauss, Professor
Department of Forest Science

PARTICIPANTS:

LEVIS HANDLEY
ROBYN ROSE
MICHAEL BLANCHETTE
CRAIG ROSELAND
MEGHAN THOMAS
HALLIE PICKHARD
JIM WHITE
LAURA BARTLEY

P R O C E E D I N G S

(4:08 p.m.)

MS. SMITH: Welcome to our Stakeholders Discussion Series on our upcoming environmental impact statement on our revised biotech regulations. We want to thank you for taking time to join us today, and we look forward to hearing your thoughts that you will be sharing with us.

There are primarily two purposes for the meetings that we have been conducting this week. The first is: to give us an opportunity to share information regarding our plans for developing an EIS and to amend our plant biotech regulations; the second is to gather diverse and informative input, which will support and inform the decision making on our part in development our new regulations.

We have here from BRS most of our management team as well as other members of the staff; and, when available, other key Agency personnel involved in supporting BRS on this effort. I do want to mention two key individuals, though, who have now been dedicated to providing full-time management of our work to complete both the EIS and our revised plant biotech regulations.

The first is John Turner, who you likely

know is a very important member of our team in BRS. I am pleased to say that John is leading this effort on a full-time basis. The second individual and likely a new face who you may not be familiar with is Dr. Michael Wach, a recent BRS hire as an environmental protection specialist within our Environmental and Ecological Analysis Unit, which is headed up Dr. Susan Koehler.

In addition to possessing a Ph.D. in environmental law and a J.D., Michael brings research and experience in plant pathology and weed science, as well as legal experience in cases involving NEPA, the Clean Water Act and Clean Air Act and other environmental laws.

At this point, I will turn the meeting over to John Turner, who will provide some additional background information; and then, when he completes his remarks, we will open it up for your comments.

MR. TURNER: Thank you, Cindy. As you may know, we have been participating in interagency discussions with the EPA and the FDA and the White House. We concluded the coordinated framework that has provided the appropriate alliance and risk-based regulatory approach for biotechnology, but that the Plant Protection Act passed in 2000 provides a unique

opportunity for APHIS to revise its regulations; and to potentially expand our authority while leveraging all of the experience we have gained over the past years in the regulation of biotechnology.

So we concluded, with some agreement, on how we would proceed with the revision of the regulations. But still there is much opportunity for input from the public and stockholders as we develop the specifics of the regulations. Given that, the purpose of this meeting is to hear your thoughts and ideas on the subject, and also to have a informal give-and-take. It is really a unique opportunity at this time because we are not yet at the formal stage of rule making, so we are free to share our ideas.

Our discussions are being professionally transcribed for two reasons. One is that we want an accurate account of the discussions in order to facilitate our ability to capture and refer to the input in the future; and secondly, in the interest of transparency and fairness, to all the stakeholders, it will be made available as part of the public record and possibly on our Web site documentation of stakeholders' discussions, so that the public and other stakeholders will have the benefit of each of the discussions that have taken place the whole week.

I want to emphasize that while we are happy to share with you at this time, the direction we are likely to be taking, the input that we get from the stakeholders and the public will be shaping that direction as we go forward. In addition, officials in the U.S., including our administrator, the undersecretary, our Office of General Counsel, and the Secretary will also be insightful in directing us as well.

So, while we value your input, we just want to remind you that this is an evolving process; and though we may have enthuiasim around one idea today, it is still an evolving process. Since it is hard to predict what the final regulation will look like, it is valuable to talk about some of the priority areas that are going to set that direction.

Those are: rigorous regulation, which thoroughly and appropriately evaluates and insures safety and is supported by strong compliance and enforcement. The second is: transparency of the regulatory process and regulatory decision making through stakeholders and the public. This is, of course, critical to public confidence.

And, of course, we want a science-based system that insures that the best science is used to

support our regulatory decision making in order to assure safety. We need communication, coordination and collaboration with a full range of stakeholders.

And finally: international leadership. We want to insure that international biotech standards are science based and dedicated to regulatory-capacity building; and we need to consider the impacts on international impacts of any domestic regulatory policy in making the decisions that we make.

With that, you can state your name and your position and who you represent; and then, we are free to start off in whatever fashion you like.

MR. STRAUSS: Thanks very much, John and Cindy. I would appreciate some give and take.

MR. TURNER: Sure.

MR. STRAUSS: The document that I have given you is from Wayne Parrett and Scott Merkle and myself. We are plant biotech scientists. Two of us work on trees but that doesn't really matter. So we would like to think that we are giving you a scientific perspective, a perspective of people who are actually doing genetic engineering of plants and think about the risks and benefits all the time.

We have also gotten a number of permits or notifications for field trials. We each have

collaborated a lot with companies of different sizes, so we have a good idea of what their perspective is; and we can speak a bit more freely than they typically can, in terms of what the science says and what we think it says.

Some day, I think, all of us will imagine that we may be involved in a public sector or lease of some trajectory somewhere down the road. So we think about: What it is going to take to get through all the hurdles? Can we possibly ever afford it? Is there enough clarity, certainty? Is there any water around?

MS. SMITH: I'll get it.

MR. STRAUSS: I am fighting a little bit of a cold as well. So we think about: What it is really going to take to jump through all the hoops without the budget of a Monsanto or somebody to do it? And there are lots and lots of minor crops out there, lots and lots of missed opportunities that, in some, are worth lots and lots of money. I am not going to quote a number because I am not an economist and I would probably get it wrong, but I know that it is vast.

So it is very important that the regulations not be so onerous that small companies and public-sector researchers just can't participate in biotechnology. That is very much in the back of our

minds. I don't have a conflict of interest in the sense that I don't have stock in the company; I don't have any releases in mind in the foreseeable future. So I really speak to you as a scientist who works with companies and who works with the science of genetic engineering.

Other comment: What I have said so far -- Wayne Parrott and myself and Scott are going to be seeking input from a number of other plant biotech scientists, perhaps many dozens. So you may see a document before your deadline for written comments that looks something like this. But, hopefully, I have support from many other scientists and it has been revised. But I simply just could not get it done in time for this, these other constraints.

If you see something that looks similar, that is not an accident. So what I propose to do is just kind of high-light some of the perspectives that we have. If you want to comment at any point, I would be really happy to do that, or perhaps at the end, we can talk about that.

I guess the first comment would be: We support what APHIS is doing in taking a fresh look at the regulations. We think that the science and technology have evolved much faster than anybody would

have expected. It is just not up to date from a strictly science point of view. I think you guys have done a great job over the years in taking what you had and using good science to make decisions. But I think it would be nice to really start fresh. So we support the notion of what you are doing. Whether we will support what comes out at the end is unclear. Time will tell.

We also strongly support that it will be a science-based method. We understand fully that there are different points of view about biotechnology and genetic engineering around the world. Inside the U.S., some people hate the concept, and some people love it, both to excess with respect to the science. But we think it really needs to be science based. There are other mechanisms in society for making other kinds of decisions.

There is a marketplace, for example. So we strongly recommend that and that is why we are glad to see that is your intention. That is one of the reasons that we are here, as scientists basically, to give you our scientific points of view. There is not one scientific point of view, of course. But we think that we have worked as closely with this stuff and thought about it as much as anybody.

One perspective that we have, which is a little different than you sometimes hear, from some of the companies involved or other scientists, is: We think there is a lot of regulatory decisions that can be made up front, sort of a case-by-case --

MR. WACH: Paradigm?

MR. STRAUSS: Thank you very much. You can send me the bill later.

MR. WACH: It's April 15th that you will be getting that bill.

MR. STRAUSS: All right. Don't remind me. We think that looking at the science, looking at the risks of different kinds of traits, different kinds of genes, that categories can be established up front that give much more clarity than we have today about what is it is going to take? What kinds of regulations, with the field testing and commercial stage, will apply?

As I have looked at regulations over the years, it has really been: You come to us, tell us what you want to do and then we will respond. It has been very reactive; and companies just simply don't know what is going to happen.

Public-sector researchers, we talk about this quite a bit. There is a bunch of discussion

going on now on the Internet with respect to deregulation, trying to figure out: What does it really cost? Monsanto says one thing; the folks in public-sector research think that it is much less in terms of price. But nobody really knows. It is just murky and I really think that you should do a lot of the intellectual work, as much as can up front and lay out what needs to be done. In a sense, I think what you are doing is deferring critical decisions, which just creates more cost and more uncertainty.

So I have talked about different things in the document that I sent you and I have written about that in the last year in a couple of publications, which I can leave with you. One is in *Science* magazine and one in *Bioscience*. In the *Science* article, I actually talked about three general risk classes. Obviously, that is just a growth level, but at least to me, it still works. Given the test of looking at it and thinking: Did I embarrass myself by writing this? I still continue to like what's there, even if you don't.

So some of the decisions that I think you can make up front and not defer, one would be with respect to classes. Define them based on scientific criteria. And, of course, the PMPs and PMIs, some of

them would probably be in the highest-risk category, in the highest frequency, but others might not be. They might be in more of a moderate-risk category. So I think that there is a lot of proteins out there that, if consumed at low levels, they are extremely little risk. That is my understanding of the science but I am not an expert in that area.

Then, in the lowest-risk category, it would be where we are really doing what breeders do but with intention and precision. For example, changing the lignin content of a tree, breeders do that already. The difference is that we would be doing it by actually looking at the genes involved and trying to turn them up or down, or sideways.

That is very much like breeding. It is not new genes; it is not gene functions. You are tweaking the regulation of genes that are already there. That goes on in nature all the time. There is tremendous genetic diversity out there right now for that same thing but it is very hard to understand it and get a handle on it. So the goal there is really to make breeding less of a craft and more of a science.

So, in terms of risk categories for novelties in the environment, to me as a biologist, that is dramatically lower than introducing a novel

protein for past resistance, a totally different category. Anyway, that is an example of some of the categories that I have in mind. But I will discuss it in more depth and there will be some grey areas between them to be sure that decisions have to be made or temporarily made, and then revised over time. But I think that would be critical.

At the lowest level, as a biologist, I think it is entirely appropriate to exempt them from regulatory overview at every stage. One of the projects I actually worked on is: How to make a dwarf tree, specifically by turning genes up or down that would slow height growth. In a forest tree, I have yet to hear anybody tell me about how that it is going to be. Could the Kudzin vine that is going to take over the world.

If it is of use to people in orchards, or perhaps to forest plantations by increasing yield per unit acre by having a dwarf tree, it is extremely low risk for invasiveness. I can't imagine it getting much lower. I don't see the logic for regulating that, particularly when we have chosen not to regulate hybrids and all kinds of other things that we do in breeding that are a much higher risk in my view.

So, I think there really are categories, and

perhaps in the beginning, they are modest categories and they grow over time. But I think right now, we could agree on some things that are very low risk in terms of spreading in the environment and might be exempted, at least at the field-testing stage, if not commercially.

Tools: There are a lot of tools we use that we have gotten very familiar with. Agrobacterium is a tool. I don't think that there is a sense that getting a little bit of extra agrobacterium DNA -- for example, you probably know that it is very common to have weed through beyond the borders. When you transfer tDNA, I don't think that creates a risk factor. But just the presence of agrobacterium DNA that might be a categorical exemption perhaps. We know that there is agrobacterium DNA in plants already that has been transferred in evolutionary history.

One other very important one, perhaps for future commercial uses, would be: gene suppression. It is a technique that you probably know called RNA interference where you take a gene and you create a double-stranded version of it and it triggers a plant mechanism for fighting off viruses and transposons and regulating development we now know that allows you to turn the expression of that gene down.

So there are many kinds of cases where you want to turn down an allergen or a toxin, or just change development by turning down a developmental gene so the plant looks different, has sweeter fruit, whatever the case might be.

It is a fairly new technique, a couple of years old. But I fail to see up front why there would be a risk to the technique at all. Of course, in the natural populations and breeding populations, what we call loss of functional alleles, where you have genes where basically they have a mutation, so they don't work or they work poorly, those are all over the place. Nature is full of them. So if we create that same geno-type through RNAi, does it constitute a risk that we are not very familiar with? I don't think so.

That is really a very important example of a tool that you may choose to deregulate right up front, particularly where you are using a native gene or a homologous gene.

MR. WACH: Steve?

MR. STRAUSS: Yes.

MR. WACH: Can I ask you what you mean by deregulation up front?

MR. STRAUSS: Yes, what do I mean by that? That means that I don't know how to process what would

work in terms of -- but I would assume the first time it ever happens -- well, perhaps you folks would have it in the regulations, where you would say: trans-genetic material that has a homologous gene. When I say homologous, I mean you can see a functionally equivalent gene in a native plant genome where you have a double-stranded version of it, with the intention of reducing the expression of that gene, that is a non-regulated article. Period.

That is what I mean, so no further consideration of it. That is like what breeders could do quite readily. Maybe not as efficiently or not with as much science because they tend to not know what genes they want to turn down for particular traits. They just look at the phenotype.

That is what I mean. Does that help? Just categorically, you have that but that wouldn't be considered in a regulatory package or in a field-test permit. And there are probably some cases where there could be additional risk involved. Where you do that, the question is: Is it any more risky than conventional breeding, which does this all the time?

One other point that I think I missed in my little notes here is: I think establishing a context, a framework: What do you compare things to? It says:

No frame of reference. You can never make a decision about anything that is done in the environment, any change of any sort. I think that your framework should be conventional breeding, which is not free of risks. But it is amazingly accepted socially throughout the world. No one has really come forward and said: Let's regulate all new plant varieties. But there are probably some groups that have said that, given the diversity out there.

But by and large, society, as it seems to me, has said clearly that the benefits of plant breeding far outweigh the risks. We are not going to intensely regulate all the products of plant breeding. Because, as I look around the world, almost nothing is regulated. There are efforts to regulate exotic plants for example, as a subset, but not the breeding process itself where you take an established plant material growing in a geography and modify it through hybridizations, through radiation, through inbreeding, through cloning, through all those things that we do that radically change the characteristics of plants.

Are the tools terminators, things that are really useful instead of just telling a transcription unit: Stop here. You can have different ones. Again, it is hard for me to see that there is much risk

involved with using one versus the other. Perhaps there is a list of ones that are commonly used that have been in crops already that have been deregulated, or studied well that one can just say: These are all non-regulated articles.

Promoters, a similar thing. So I think the 35S promoter, which is one example, is itself not viewed as being a risk factor. It can turn up some genes very high. If you have a novel gene turned up very high, that may be a risk factor. But the promoter, itself, probably wouldn't be. So that would be another example.

Other ones that occured to me, and again, I didn't put together a long list. Barnase and barstar are genes that you know that have been used for making male sterile plants. I think those are non-toxic proteins. I believe they are rapidly degraded in the human gut like most proteins are. They are very useful for a variety of purposes. When you want to take a tissue and destroy some subtypes of it, in one case you get a male sterile plant. There could be other cases as well.

So that may be a tool, basically an ablation tool. and the barstar, basically can reverse it for breeding purposes, or say we have a project where we

are trying to create sterile trees and we are worried that the barnase will be leaky, meaning it will express in vegetative tissues as well as floral tissues and make our trees shift. We have some evidence of that. So what we are doing is actually expressing a little bit of them in a background level throughout the plant. It is like a little sponge to soak it up. That seems to be working very well.

That is just an example. Are these proteins dangerous in any way? I don't think so. These might be tools that might go in that bag of things that are deregulated and there are probably other good examples.

Finally, in terms of decisions that might be made up front are: the genetic-engineering process itself. You have heard time after time and time again, that it is the product, not the process. It is about time that we got serious about actually putting that into regulations, saying for example: It is not the process of genetic engineering. It is not what genetic engineering does. So when you insert a gene, you go through the tissue-culture process and you put a gene in, you do create changes in the genome.

My proposal is that should not be regulated because you can do similar things with non-GE

techniques that, as far as you can tell now, are just as dramatic. You can make a hybrid and they cause changes in the genome, duplications and deletions and changes in gene expression. You can inbreed and force the expression of very rare genes that could be coat (ph) for toxins and other kinds of things.

Of course, now, if a tulip breeder eradicates their seeds to get more color variety, completely unregulated. Yet, they are making lots of changes in the genome.

MR. TURNER: So, if you did go that route and decided that you wanted to be a purist and not regulate it according to the process --

MR. STRAUSS: Yes.

MR. TURNER: -- how then do you avoid not regulating those other types of things that people generally put into traditional breeding that, as you said, are socially acceptable and all?

MR. STRAUSS: Perhaps the regulation is more like in Canada where you regulate according to the novelty of the trait or the product and not the process. I guess that is what I am recommending; and, of course, that is whole change in orientation, right?

So the trigger would be completely different. That is really radical but maybe the

trigger is the same, but then you very quickly have classes. You have the GE trigger but then if you are dealing a homologous gene, you immediately go to an exemption or an intention to examine some more data or, depending on the particular category, that is what I would imagine happening.

But that is really very critical. In mutagenesis, when you do deviate, you create more genetic diversity. And GE is genetic engineering, if I can define that. You have probably heard that before.

MS. SMITH: Once or twice.

MR. STRAUSS: Yes. Breeders would like to take advantage of that. That is more diversity for them. If they are doing all this rigorous field testing, they are going to see some variances that are different and they want to take advantage of that. They don't want to have to select the things that look exactly like the progenitor plant because of substantial equivalence, or other regulations.

They would like to introduce the new trait. And then if there are other traits in the organism that happen at the same time and they see them in field trials, there should be no reason that they can't take advantage of that.

The other aspect of that that we worry about a lot is: Are you regulating events, or are you regulating the novel phenotype caused by the novel gene? Now, I don't see the logic to regulating events. People, like me who think about trees and imagine that it is going to be transgenic, heterozygous-transgeneic clones that are produced, you don't want to think about a new regulatory package for each event. And the event --

MR. TURNER: And that's based on -- it is just the insertional mutagenesis that happens.

MR. STRAUSS: Exactly, all the time.

MR. TURNER: Is that your assertion?

MR. STRAUSS: Yes, exactly, right. And the deregulation for the gene could have brackets of expression. For example, every event also gives you different levels of trans-gene expression, which could be significant.

So someone coming forward might want to, for example, have 10 different events that have expression that goes from one to 100; and basically, if you tried to get deregulation for that whole set of variability, but the background is irrelevant. It is just a transgene expression of this amount versus that amount. Do you know what I mean?

You are trying to cover -- what differs in events is the extent and the specific pattern of transgene expression. So that you might need to account for in some way, particularly if you are introducing a gene. If you have too much of it, it is bad. If you have too little of it, it doesn't do the trait. You may have to worry about that. But I suspect that most of the time companies are going to take the worst case and say: You know this gene is just harmless at any level. It is a protein that is produced by it. I am just trying to focus. I am not trans-gene expression per se.

I am just saying that that has to be addressed. What is the level of expression you want? For instance, if it is a novel protein, what is the industrial level of expression that you need to worry about? But given that you have done that, given you have said that the level of expression can vary from one to 100 and we considered that, the background stuff doesn't matter. And that means, for example, that it is probably not necessary to worry about having a single copy versus multi-copy events.

Now, most breeders want single copy events because they are simpler. Because they probably are less prone to close suppression where genes get turned

off. But in my experience, at least with vegetatively-propagated crops, the correlation between copy numbers, the number of insertions and stability, is almost zero. It is very low. It is something that scientists talk about but breeders don't worry about.

So, if I have a really good multi-copy event, high levels of expression, stable expression, but now I had to go and sequence around every insertion and look at: What is the surrounding DNA? How has it been changed? That increases cost a great deal. If I had to worry about: What if I landed inside of a gene, how have we changed it? That increase costs a great deal.

My argument is basically: That happens in breeding all the time, all the time. So why are we worrying about it with GE when we're not in normal breeding? That is basically the argument.

So the mutagenesis aspect of GE, I think is something that you might consider deregulating with reference to conventional breeding where we accept all kinds of mutagenesis. That is the proposal. Then, if you do that, there are sort of follow-on conclusions like: Do we need to worry about copy number? Do we need to characterize each insert in terms of where it is in the genome and what has been affected? Probably

not.

These are things that will basically reduce costs and I think don't add much in terms of risk analysis. That it why it is important from the point of view particularly of a small company or a public-sector researcher. If you want to release 20 different transgenic products and they each have several insertions, that is a lot of work to characterize them. And then when you do characterize them, what do you do with that data? What does it tell you? How do you interpret that? Why collect data that you don't know what to do with? You collect no such data in conventional breeding and we are certain that the same kinds of effects are happening.

We know that now the last few years of study. If you compare different individuals you'd be amazed. You'd see it is very common for certain genes to be deleted in one genotype versus another. It is an extraordinary thing when you sequence large sections of genome, you see that. So why are we worried about the loss of function of a gene through GE when, in breeding, that happens all the time. I am probably beating this dead horse a little bit too much. But it quite important that if you do accept that a mutagenesis of GE is not the issue, there are

some fulsome knock-on conclusions you make that are different than how we are regulating now, as far as I understand it.

MR. WACH: Is your argument that it happens or that you don't have to worry about that it happens?

MR. STRAUSS: It happens and the risk from it, based on breeding, is very, very low.

MR. WACH: Is it because the variety wouldn't get any further in a breeder's eyes, if your insertional event knocked out some other useful or essential gene?

MR. STRAUSS: You know what? I think it is Mike and I think this whole knowledge base is progressing, but in programs where you intentionally try to knock out a gene to see if the it is roughly half of the knock-outs give you any observable phenotype.

So if you take a whole bunch of arabidopses and knock out a gene one by one and grow them, half of them they look exactly the same. And I suspect their chemistry is very, very much the same. I think it is because plants are very redundant canalized (ph) organisms. They are used to getting insults from the environment, including mutations and they still do their thing.

So it is actually much harder to change them than we used to think. They are very resistant to large changes, and that is probably why it very safe in breeding. Very rarely do you see an event that gives you a large change in chemistry that creates a toxic potato or celery. It happens every now and then, but it doesn't happen very much. There are other things in the breeding process that seem to be able to catch it. They taste bad, or a farm workers' hands get sore, so you throw it out. So does it have to be regulated up front? And do you want to regulate it at the molecular level?

Perhaps you want to regulate it, as breeders, in effect, really do, by looking at the chemistry of the plants and the new varieties. But that is not done by the federal government looking at the DNA structure. It is done by breeders out there in the world who are worried about their product and lawsuits. So do we need it at all, even at the phenotypic level?

I don't know if I answered the question.

MR. WACH: You did exactly?

MR. STRAUSS: Yes. So, in keeping with this notion that there are classes that we can make, classes and subclasses, the adventitious-presence

issue, which you brought up, I was very glad to see. That is just critical. Agriculture is messy. Agriculture is not rocket science in the sense of keeping things clearly labeled and segregated in the real world and it never will be. For the really high-risk PMI and PME plants, it has to be pretty close. For a lot of the PMI and PME plants, it probably doesn't have to be, although there are public-perception issues and all that kind of stuff involved; and scientific issues of how you make decisions about what is low and high risk without a lot of data experience. I recognize that.

But the adventitious presence really — and these need to be laws, I believe. I am not a lawyer, so I am on very dangerous ground here. But these just can't be interpretations that you make because people are going to sue and already are, over this kind of stuff. For example, if a company has modified lignin in a tree a few percent and they get a faster growing tree and someone down the block sues them, then they can't do it. If the tolerance is zero, no grower will even risk it at all. It is a no go.

If, on the other hand, we said: This is really a lot like breeding. It is a little more precise. It is not the process. It is the result

that matters. The tolerance for presence is 100 percent, or it is 90 percent or it's 10 percent. But it is something easy and high. It is just like growing trees in separate places. You will be able to deal with that in most cases.

That is radically different that people can go ahead and do it. If you don't have those tolerances at reasonable levels, there is gigantic classes of genetic engineering that won't ever be pursued because the benefits aren't great enough and you can't tolerate the risks of someone suing you over some unintended presence.

And I don't know if you are talking with the White House about actually changing some of the laws about this. So my understanding is that the FDA has a very short list of adulterations in food. It's those things and nothing else. If you had a new PMI/PMP show up in foods that is an adulterant. Period. At any level.

Am I correct about this or am I □

MR. TURNER: They have a long list of things which are not adulterants.

MR. STRAUSS: Okay.

MR. TURNER: But things that have GRAS status, so □

MR. STRAUSS: Right. That kind of stuff.

MR. TURNER: If it is not approved and it is an adulterant or it can be clarified as an adulterant, so that is the way that works.

MR. STRAUSS: Right.

MR. TURNER: Somewhat that idea.

MR. STRAUSS: Yes, it's the same idea. What we need perhaps is a process where some of these PMI/PMP genes are recognized as not being adulterants, or basically a tolerance is set. My understanding, again as a basic biological scientist, is that there are lots of classes of PMI/PMP things that are going to be exceedingly low risk when consumed if they are not injected. And those would be logical things that have tolerances that are not one part protrilyn (ph) but something considerably higher.

If we do that, then we open up an entire field of industry with, as you know, extraordinary benefits for consumers for medical products of various kinds, or industrial products. If we don't do that, I doubt those things are going to go forward at all. So it is very, very important.

MR. WACH: What do you currently do in your research to ease the concerns of the general public who live nearby? What has been successful for you in

your community?

MR. STRAUSS: I have never had a case, well, except I had one case where some people came and cut down some trees in the middle of the night. But I have never had a case where the community has come by and said: Explain to us what you are doing? Give us the gory details of it.

When I talk to students and so forth -- and for me this is very important as well for very personal reasons. I work on genetic engineering as sterility as a containment strategy in trees. I do other things as well, but that is a fairly core project that we have worked on for many years.

Well, trees have to flower to observe it. In any kind of research, there is never 100 per cent success. If there is, then you don't know why you were successful. So there needs to be some genes released into the environment. And if they are trees, it is not going to be just the pollen falling next to them. There is going to be some release out there.

For example, if the interpretation was that no adventitious presence of a gene in a poplar tree a mile away was allowed, we couldn't develop that technology. We couldn't afford to create greenhouses that are 40 feet high and grow trees in them. Even if

we did, that probably wouldn't be very satisfactory because it hasn't been in the environment and the environment varies dramatically.

So to do the research that I do, we need basically the informal tolerance for adventitious presence that you have now. If that changed, if that became a zero or a very, very low level just because of the transgene, then we are out of business. I don't see how anyone else is really going to develop transgenic-sterility mechanisms and really rigorously test them anywhere except for perhaps on islands or some place with 100 miles of water between them. And even that isn't quite good enough. Pollen can move over incredibly long distances.

Anyway, I really haven't had an issue yet. But what I would say if someone asked me: Aren't you contaminating the environment, I would say these are sterility transgenes. If they work well, they reduce fitness. That is not something that helps the tree get more fit. And we don't release genes like that that don't have that kind of pretty clear characteristic of reduced chances for spread. That is only going to be used in trees, at least in my hands, when it is allowed and when we really have a tight sterility system, which is perhaps quite a few years

down the road, if ever.

So that is the kind of general thinking that I would have.

Other comments that I have in response to the *Federal Register* questions: interstate movement. It is a pain in the neck following all these things. It is very hard for academic and public-sector laboratories that don't have a regulatory-science division to keep track of all these things. So what you should be doing is regulating things that are important rather than everything just based on methods. For example, in my case, vegetative propagules, in general, things in tissue culture, cuttings, things that in almost no cases, at least for the plants that I work with, can they establish on the ground without somebody planting them and taking care of them. It is very different from seeds. When you drop a few seeds and they have a good chance of establishing somewhere.

So the proposal I have in what I gave you is: low- and moderate-risk materials and maybe vegetative propagules that can establish should be deregulated for everything, apart from the really high-risk PMP/PMIs. Did I get the acronym right?

MS. SMITH: Yes, PMI is fine.

MR. STRAUSS: Okay. Apart from stuff that you don't really want to get out at all because if that was confused with whatever the plant was, there could be some significant problems. I don't know if there are any cases like that by the way. Are there any of these plants that are so toxic that you wouldn't want any escape in the environment? I assume there are. Is there spider venom in a plant? Probably not. That is probably just in animals, right? So it would be things of that category but I don't know what they are.

MR. TURNER: There are plants that are still being regulated by and large, that have not had the food-safety evaluations.

MR. STRAUSS: Right.

MR. TURNER: Or have not been fully evaluated.

MR. STRAUSS: At all.

MR. TURNER: As you know, the vast majority will in the end probably not to be.

MR. STRAUSS: Right, and it hasn't been done yet.

MR. TURNER: So it is back to: What can you say up front --

MR. STRAUSS: Right.

MR. TURNER: -- versus what are the regulations that take place like?

MR. STRAUSS: I said, in the written material I gave you, that I would expect that you could throw them into broad, meaning many order of magnitude risk categories, based on things like, sort of like what is done by EPA for pest-resistant proteins: Does it digest readily in the gut? Does it look like an allergen in any way? Things like that that might give you fairly high comfort about low-level exposures. Perhaps that is one thing that we could do up front.

Then, over time, as you really learn how toxicology was really done, then you could perhaps change the adventitious presence tolerance. But in the beginning, perhaps you consider it as something higher than zero based on some of these early screens. I would imagine one could do that with high confidence, but I am not an expert in that area, so I perhaps better move on.

I was talking about interstate movement. We do a lot of that, arabidopsis in strains, in-vitro culture. Arabidopsis, I guess, is already exempt. Again, I would do this based on these risk categories. So if we had transgenetic poplars, where we randomly modified the expression of native genes, basically

like a mutagenesis population for identifying genes, do they present a risk?

In my biological background, when you take an organism and you screw up its gene expression for the sake of science, you don't create a better organism, you create a sicker organism in 99 million times out of a 100 million. So should that be regulated? I don't think so. So why bother keeping track of it. It is things of that sort. I have more examples in the written material.

MS. BARTLEY: Have you thought much about the Trojan gene idea and what your domesticated traits are going to do to things growing freely, or things and plants in other people's □

MR. STRAUSS: The only thing that I put in there about that is I think you are still going to need to consider endangered species. I am sure you do, legally. So if you have a large planting of something with a domestication gene next to a small population, or the last population of some □ like walnut in California. Is that what you mean?

MS. BARTLEY: Well, that is a start.

MR. STRAUSS: Right.

MS. BARTLEY: But going beyond a designated species. I think someone would be really upset if all

the cottonwoods that grew around the Creek, because they were substage and were malignant, suddenly fell over, fell over and were being left alone.

MR. STRAUSS: Right. That can happen now with breeding. We are breeding things that grow really fast, get really tall. Wind storms blow over trees quite a bit. I've seen them in plantations; I've seen them on top of was that because of breeding? Is that because hybrids are used versus not? So we do what you are saying already in terms of traditional domestication.

One other thing that I do have on my list in what I gave you is: For me that is a tremendous risk benefit or something which reduces risk a great deal is that with the trees that I work with, there are huge wild populations out there and there will be for the foreseeable future.

For example, if you thought about what proportion of wild Loblolly pines could become transgeneic over the next 50 years in the world, it is a very small proportion. Most of the ones in plantations don't flower very much. We can do calculations about that and get it right by an order of magnitude of three or four. So there is going to be vast swamping; and, as you know, for every pollen

grain or for every seed and pine, one out of a billion actually survives to be a tree. There is tremendous natural selection.

I think somewhere downstream there are going to be species now -- perhaps walnut in California is like that, according to Norm Ellstrand. Where the population is just small enough and the orchards are big enough that you need to worry now about domestication genes. So you want a sterility gene that stops it, not a domestication gene. I agree with that. But, at least with most of the forest species that I work with, pines and poplars, particularly in the United States, you would have a hell of a time even seeing a change until the next 20 or 30 years. So somewhere down the pike, it might be an issue.

But the whole notion that because you have gene flow between wild and breed populations that is more of a risk factor. I think when it comes to what I am calling domestication genes, where you tweak the expression of native genes, I see that as a benefit compared to say covering the world in an engineered specie that is domesticated and there isn't a wild population buffer. There is a very small one. Then you can swamp it very easily.

That is really different for trees and that

is place where, from my view, the public has kind of a perception that well, it is a perception that applies to all GMO things as though they are all equally risky. The notion that a gene is going to come out and spread and take over the world. For some genes, there are risks that are credible. So for the BT gene, we worry about that. We can talk about that well into the night and why it may not be much of a risk. But we definitely would give it serious worry. Whereas, for a dwarfism gene, given that you have large wild populations, I just can't see how you could even get into the ballpark of worry, at least not for decades and decades.

So one of the issues that I suggest is that you consider the scale of release and the many ways that mitigation happens above the gene level when you make your decisions. If you had sterile trees planted but they occupied one percent of the acreage of Loblolly pine, do they really have a significant impact on wild populations of anything?

Right now, when we grow trees, you plant them at high density. They don't do a lot of flowering, much, much less. That probably has a much bigger impact than anything we would do with a GE tree for a long time. Again, considering the scale is very

important.

MR. WACH: Talking about doing up-front regulation, just based on what you are talking about the dozens of ideas of the things that are possible, we do have an enumerated list of things that you don't have to worry about these any more.

MR. STRAUSS: Yes.

MR. WACH: But in terms of you planning your research for the next 10 years, or someone who is just starting their career and planing their research for the next 30 years, we couldn't possibly enumerate and make a useful list for that person. How can you plan your research if we can't possibly reassure you that what you are doing is going to be deregulated down the road?

MR. STRAUSS: Right.

MR. WACH: So how do we balance; how do we come up with up-front regulations that give you every assurance but also accommodate the growing technology?

MR. STRAUSS: Yes. I do think, Mike, that there is always going to be a class of things that are new. That is what science does. They are going to have to tell you why it is safe. You can't tell them if it is safe or not up front. So I think that that is always going to exist. You are always going to

have to react to some things.

But what I am recommending is that there are a bunch of tools that people will want to use repeatedly. I forgot to mention some of them, such as the GUS-marker gene, or other marker genes where we already have a lot of safety information about, which respect to consumption and presence in the environment.

And you have got acquiescent genes, certain ones. The NPT2 gene is something that, as far as we can tell, has a tremendous safety profile. If you think about what the alternatives are to get rid of genes, they raise a lot of risks. You might have seen that there was a paper by Konig. How do you say that? In *Nature Biotechnology*, an issue or two ago, which I happened to review. He makes the point that if we throw those out categorically, the ones that are coming down stream have a lot of questions about them; the combination-gene, what do they do to the genome? How stable are they? How well can we control them?

The fact is that for most crops, we just don't have the technology yet. Transformation technology takes years and years to develop, let alone to get comfortable with from a bio-safety viewpoint. That might be one other one that you may want to

consider seriously deregulating, the specific anti-biotic resistant gene.

A paper just came out from a British society of toxicologists which I cited in what I sent. It basically says: All anti-biotic resistant genes have an incredible safety profile, all of them. They still recommend that we stick with the ones we know well, with the ones that don't have human uses or vegetarian uses. Just be prudent. They really said that they all fine because of all the different safety levels and their presence in the prokaryotic gene poll and all the arguments that you have heard before.

Again, when we are talking about science, I realize that antibiotic-resistance genes are not a feel good kind of technology. But if you actually came out and said: Science says these are safe. That would be pretty huge. People who are marketing GMO crops may choose to avoid them. People who are selling them to Europe, probably would.

But I think if you are going to have science-based regulations, some of these marker genes, both the selectible-marker genes and the reporter genes, things like antibiotic resistance, things like GUS. I don't know how GFP figures in all this stuff, but these are things you might consider having a

serious look at.

Of course, if you have these things, then one of the things that is in the *Federal Register* is techno-monitoring. Then monitoring at least presence becomes a lot easier. For example, if we put out a sterile tree, which we thought was sterile, and you said: Well, it has got to be sterile at least to this level, how are you going to monitor and prove that? If we could do it with the reporter gene, it is going to be much, much easier and much, much cheaper than it would be than if you had to go and do molecular analysis. So that would be very helpful.

MR. WACH: A corollary to my previous question?

MR. STRAUSS: Yes.

MR. WACH: Is the enumeration and I see the logic in what you are saying. The amount of up-front thinking and the amount of up-front work for us will increase to do that.

MR. STRAUSS: Yes.

MR. WACH: My concern is that we will put a lot of work into a list that won't actually end up helping. It will either be too short because we have to think of a lot --

MR. STRAUSS: Yes.

MR. WACH: -- and wemake absolutely sure that everything that is on this list should be there. Then we will put it out after a lot of sweat and tears and it may actually help.

MR. STRAUSS: It won't help because it is too short, or because of the technologies that have gone by already?

MR. TURNER: Right. But you see a complete deregulation. Something that is just a marker gene or a could be called a -- I believe that we have had petitions we see things where the that went into a different variety than they said: mixed up and then how do you know that only that went in? Do you see a compromise there? How do you see that?

MR. STRAUSS: So is the question, John: Am I recommending a sort of blanket categorical, no matter what? This marker gene is okay versus a very specific?

MR. TURNER: Well, you could categorically say they are exempt. But if you have to produce a small package of documents, a couple of slides to show that it is just this or something.

MR. STRAUSS: Right. Again, if there is not a reason to do it and if you said that this gene, this protein is safe, I think any of the thousands of

proteins that are digested and it is completely safe, it has no value in the environment as far as we can tell, then I think that you don't want to regulate it at all.

I think that there has been a tendency, as I have seen it, for sort of regulations that if you do a little bit of something and then you say: Well, what about that case? Do you know what I mean? It just grows, so I think you have got to say: If the science says that it shouldn't be regulated, you don't want a permission about it.

That is what I think and the list I am thinking about is a pretty short list. I am not thinking about every antibiotic-resistance gene, for example. I am thinking about NPT2, maybe tetracycline resistance. We know that there are lots of genes out there in the environment. Two or three things that would be that small tool kit would be very valuable, that people could produce GE plants and not worry about them, that would be very valuable.

And whether in the marketplace everybody would avoid it anyway because of the stigma, I think that that could very well be; and then what you are saying is true. It would be a lot of work. But I guess I think that you have to follow the science.

That is the decision that you have to make.

And maybe eventually people will come down and come back around and get more comfortable after this initial sort of frenzy that perhaps we are in. If you think about the kinds sold in Europe, you know if all antibiotic resistance genes if all the NPT2 stuff is excluded, it has to be just out of their market, that is going to be a big deal for a lot of our products in the United States.

I think it really is something for the United States to say: We have looked at the science and just does not make sense. I realize that that is a bold thing to do and has political implications but I am speaking as a scientist now.

MR. TURNER: There are those who have been saying that we have been doing that.

MR. STRAUSS: Yes, right.

MS. SMITH: That's right.

MR. STRAUSS: There you go.

MR. TURNER: Well, you have.

MR. STRAUSS: You've tried anyway. In getting towards the end of this list, the notion of regulating non-viable GE materials. If we had to in the case of a tree experiment, clean up every piece of foliage and bark and roots in the ground, there would

be no GE anything.

MR. TURNER: That is a very broad, open-ended question.

MR. STRAUSS: Yes.

MR. TURNER: We are asking: Should we and if so, what cases?

MR. STRAUSS: And the only case would be where you had something that was really degraded in the environment in a radically different way. I don't know of any cases like that. BT wouldn't fit in my criteria when you get these tiny amounts left on particles in sterile soilS, I guess. So I don't know of any cases like that.

MR. TURNER: Highly toxic compounds, do you mean?

MR. STRAUSS: Right.

MR. TURNER: Is the question?

MR. STRAUSS: Right. So if you had something which and what do you compare it to? So, right now, we can go in the tree plantation and plant pines or poplars or maples and they all degrade at radically different rates with radically different non-target effects.

So what is big enough to be really outside of the norm? That is another question. In soil

environments, there is so much redundancy; there are so many different species that degrade, so many different things; there are so many generalists that I think that that would very much be the exception. You would have a hard time finding such a magical thing from GE.

So my sense is that it would only be in very exceptional cases where the bio-chem co-characteristics of the plant matter are radically different. Don't break down or take twice as long to break down as anything that you have ever seen in non-GE material.

If you just look at wood versus foliage, there are so many and there is such a radical variations out there in rate of breakdown as it is, to get something that is really radically different, it is going to have a big environmental protobation (ph). I have a hard time imagining what it is going to be. It could be perhaps something full of plastic, a plant that produces huge amounts of a plastic precursor. Maybe that doesn't break down very fast. But that's probably wrong. It probably does.

So I don't have any answers, John. I just think that you certainly shouldn't do it for all GE stuff. That would be radical. As far as I can see,

you would put the whole field-test industry out of business. So it should only be in very special cases.

I already said that you need a framework for comparison. You just can't be out there saying: Is it good or bad for the environment? You have to have something that you can compare it to. I hope that that is conventional breeding because that is what feeds most of the world. I respect organic food but that is still very much of a niche. I don't think that can be the frame of reference. I think it should be conventional breeding, conventional agriculture. Of course, that is very variable as well but that has got to be the starting point, in my view.

And I have talked about the wild populations and the scales of consideration for benefits and for mitigation rather than just on a plant-by-plant basis when you consider a change in a trait. Anyway, I will stop there. I enjoyed the comments that you have made and any others I would be glad to hear.

MR. TURNER: It's been helpful and we heard unique perspectives from everyone who comes in. You have certainly given me some ideas. Thank you.

MS. BARTLEY: I have another question. With RNAi and anti-sensitivity technology, have you ever seen anyone do any studies about sensitivity to viral

infection and different things that might be coopting (ph) by using that technology?

MR. STRAUSS: So by getting the RNAi system going in a plant, are you changing its --

MS. BARTLEY: Susceptibility to viruses?

MR. STRAUSS: -- viral susceptibility?

MR. WHITE: What's your hypothesis?

MR. STRAUSS: RNAi is a sequence system in plant viruses are generally -- do not have sequences homologoud to the genome.

MS. BARTLEY: The machinery that carries out RNAi is the same, independent of --

MR. STRAUSS: It is triggered by a sequence that is a double strand of molecules.

MS. BARTLEY: I know but the nucleus is the same, so you might overrun the system if you --

MR. STRAUSS: So if you actually knocked out part of the system.

MS. BARTLEY: Right.

MR. WHITE: So you're just adding one more RNAi hybrids or thousands that currently exist --

MS. BARTLEY: I'm just curious. I'm just asking the question: If --

MR. WHITE: -- asking that as a question --

MR. STRAUSS: I don't know of any cases. I

would have said what Ginger said that the expectation is it doesn't happen because it is sequence-specific and it restricted to genes or closely related to gene families. So I haven't heard of such a thing.

RNAi is fairly new in the sense of that you don't have a lot of it. Anti-sense is not new; anti-sense is very old. Anti-sense is probably RNAi.

MS. BARTLEY: We don't understand completely.

MR. STRAUSS: What is that?

MS. BARTLEY: We don't understand it completely. We don't have other blackboard pieces.

MR. STRAUSS: Right. Certainly, compared to a few years ago, the world is radically different in terms of understanding of RNAi and they are associated with small RNAi's and so forth.

Whereas, for 10 or 15 years, anti-sense is kind of like this black box of magic that no one had an idea of what was going on and what the rules were to make it work more efficiently? So there is a lot of stuff to still be learned in molecular detail, but it would be very surprising if RNAi were to have general effects on the plant. That's all and I would have to agree with Jim about that. I wouldn't exclude it completely but that would be surprising.

But there are a lot of laboratories around

doing that and a lot of it is just being published now, as you know. That would be something where you might want to if you were to consider that as a class that is deregulated, you might want to take a look around and talk to some of the laboratories and see if they are seeing anything like that. I haven't heard anything.

MR. WACH: One last question?

MR. STRAUSS: Yes.

MR. WACH: Because you are an expert, I just want to get your opinion of it. One of the criteria we use when we evaluate genetic material is: If it is coding or non-coding? In some papers that I read recently -- there was a big multi-paper piece in *Scientific America* that appeared last year about our current notion of what coding and non-coding means and the importance of that has radical changed very suddenly.

MR. STRAUSS: Right.

MR. WACH: And I am curious: What is your opinion of that growing theory of what does it mean to be non-coded and do we have to worry about what we always in the past as to what non-coding means?

MR. STRAUSS: Yes. I have always been uncomfortable with the term: Junk DNA because you

couldn't have all that DNA and have it do absolutely nothing, so it was doing stuff. I'm starting to appreciate all the different ways it takes place in regulation; and, of course, now we are seeing things like micro-RNAi's are one class of genes that we weren't recognizing before at all that are in the genome.

So there is just a lot to be learned about that.

MR. WACH: Why don't we say that in our comments.

MR. STRAUSS: What's that.

MR. WACH: I said that we'll get that in our comments, I'm sure

MR. STRAUSS: Right. Yes, the thing that you have to have is a frame of reference. So one thing that your regulation should very much do is take a look at genome science and look at the structure of genomes. We have these DNA sequences now and we know how genes move around and get interrupted and turned around; and promoters move and enhancers act from ten kilobases away.

There is just so much fun going on, I guess. The gnomes are so fluid that that is kind of the background. That is just conventional breeding and

genetic diversity is vast. So when we do something through genetic engineering, we do change some of that balance. I wasn't saying you don't. You do. But the question is: Are you changing it in a radically way that has more risk than what you do in breeding? And I don't see that.

We are never going to know every detail of how the genome and how the non-coding DNA works, at least not for a very long time. But I think that the scientists I talk to cannot see a reason why genetic engineering is much, much more risky than conventional breeding, particularly because breeders they slam plants. They do a lot of stuff to generate diversity. That's what they do. And now and then, they throw out 99 percent of it.

MS. SMITH: Okay. Thank you very much for coming in. This has been a really unique perspective and kind of a nice one to close on, actually.

MR. STRAUSS: Have a good weekend. Sorry to keep you so late. I do apologize for that.

MS. SMITH: It's okay. It kept us awake.

MR. STRAUSS: Thank you. Good luck.

(Whereupon, at 5:19 p.m., the meeting in the above-entitled matter was concluded.)

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REPORTER'S CERTIFICATE

CASE TITLE: STAKEHOLDERS MEETING WITH OREGON STATE UNIVERSITY

HEARING DATE: February 27, 2004

LOCATION: Riverdale, Maryland

I hereby certify that the proceedings and evidence are contained fully and accurately on the tapes and notes reported by me at the hearing in the above case before the United States Department of Agriculture.

Date: February 27, 2004

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